



## General

### Guideline Title

Herpes viruses. In: British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011.

### Bibliographic Source(s)

Williams I, Leen C, Barton S. Herpes virus. In: British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011. HIV Med. 2011 Sep;12(Suppl 2):61-9. [84 references]

### Guideline Status

This is the current release of the guideline.

## Recommendations

### Major Recommendations

Level of evidence (I–IV) ratings are defined at the end of the "Major Recommendations" field.

#### Varicella Zoster Virus (VZV)

##### Treatment

##### *Zoster*

- For localised dermatomal herpes zoster, oral aciclovir at a dose of 800 mg 5 times per day is recommended. Famciclovir and valaciclovir are alternative agents although data to support their use has thus far only been available in meetings abstracts (Sullivan et al., 1997; Brentjens et al., 2003), but they may be preferred by some because of the more convenient dosing and their ability to cause higher antiviral levels in the blood as discussed in other guidelines (Dworkin et al., 2007). For severe cutaneous disease or disseminated herpes zoster infection with evidence of visceral involvement, including central nervous system (CNS) disease, admission to hospital and treatment with intravenous (iv) aciclovir (10 mg/kg every 8 h) is recommended (Balfour et al., 1983; Shepp, Dandliker, & Meyers, 1986) and 10–14 days of treatment is usually required, based on the experience in human immunodeficiency virus (HIV)-seronegative immunocompromised individuals (III).
- Patients presenting with disseminated herpes zoster infection with visceral involvement should be started on highly active antiretroviral therapy (HAART) or current antiretroviral therapy (ART) optimized to improve the level of immune deficiency (IV).

#### Herpes Simplex Virus (HSV) Infection

## Diagnosis

### *CNS Disease*

- Polymerase chain reaction (PCR) for HSV deoxyribonucleic acid (DNA) in the cerebrospinal fluid (CSF) is the diagnostic method of choice for diagnosis of HSV encephalitis or meningitis (III).

## Treatment

### *Orolabial Herpes*

- First episode or severe recurrent orolabial herpes infection should be treated with antiviral therapy. Aciclovir 200–400 mg orally 5 times a day for 7–10 days is recommended (II). Alternative treatments are valaciclovir or famciclovir. For severe oral mucocutaneous disease treatment should be initiated with aciclovir intravenously 5–10 mg/kg every 8 h (III).
- There is not comparable data for the use of valaciclovir in treatment but on the basis of its activity in other settings and its efficacy in preventing recurrence of HSV in HIV-seropositive individuals (DeJesus et al., 2003) many clinicians would consider it as an alternative to aciclovir or famciclovir (IV).

### *Genital Herpes*

#### First-Episode Genital Herpes

- In view of the potential for more severe disease, prompt treatment with aciclovir 400 mg orally, 5 times daily for 7 to 10 days is recommended (Romanowski et al., 2000) (II). Alternative regimens are valaciclovir 1 g orally twice daily for 5 to 10 days or famciclovir 250–750 mg orally 3 times daily (tid) for 10 days, but as above, the recommendations for valaciclovir are extrapolated from other settings (IV). In patients with severe cutaneous disease or systemic complications, aciclovir 5–10 mg/kg iv every 8 h should be considered (III).

#### Recurrent Genital Herpes

- Recommended regimens for suppressive antiviral therapy include: aciclovir 400–800 mg orally 2 or 3 times a day (Ia); valaciclovir 500 mg orally twice daily; or famciclovir 500 mg orally twice daily (Ib).

### *Antiviral-Resistant HSV Infection*

- Any immunocompromised HIV patient developing clinical HSV lesions despite adequate doses of aciclovir, valaciclovir or famciclovir must have a sample taken for viral culture and testing for antiviral sensitivity. If new lesions are forming after 5 days, despite increasing the doses of antiviral drugs then therapy should be reviewed and changed (IV).
- Systemic therapy with either iv foscarnet 40 mg/kg bd or tid iv has been shown to be effective for aciclovir resistant strains with the length of therapy depending on treatment response (Safrin et al., 1991; Hardy, 1992) (Ib). In rare cases with aciclovir and foscarnet resistance cidofovir topically (Snoeck et al., 1994) or iv 5 mg/kg weekly infusion is the preferred agent (Saint-Léger et al., 2001) (III).

## ART

- In patients with prolonged cutaneous ulceration or who have systemic disease, consideration should be given to initiating combination ART or changing therapy in those experiencing virological failure (IV).

### Definitions:

#### Level of Evidence

Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

- Herpes virus infection
  - Varicella zoster virus (VZV) infection
  - Herpes simplex virus (HSV) infection, including orolabial herpes and genital herpes
- Human immunodeficiency virus (HIV) seropositivity

### Guideline Category

Diagnosis

Management

Treatment

### Clinical Specialty

Dermatology

Family Practice

Infectious Diseases

Internal Medicine

Pathology

Preventive Medicine

### Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

### Guideline Objective(s)

To help physicians in the United Kingdom investigate and manage human immunodeficiency virus (HIV)-seropositive patients suspected of or having a herpes virus infection

### Target Population

Human immunodeficiency virus (HIV)-seropositive patients suspected of or having a herpes virus infection

# Interventions and Practices Considered

## Diagnosis

Polymerase chain reaction (PCR) for herpes simplex virus (HSV) deoxyribonucleic acid (DNA) in cerebral spinal fluid (CSF)

## Treatment

1. Varicella zoster virus (VZV) infection
  - Aciclovir
  - Famciclovir
  - Valaciclovir
  - Hospital admission for severe disease
  - Highly active antiretroviral therapy (HAART)
2. HSV infection
  - Aciclovir
  - Famciclovir
  - Valaciclovir
  - Foscarnet
  - Cidofovir
  - Suppressive antiviral therapy for recurrent genital herpes
  - Initiation of antiretroviral therapy (ART) or changing therapy

# Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Prevalence rate of herpes virus infection
- Risk of transmission of infection
- Response rate
- Recurrence rate
- Morbidity and mortality
- Resolution of infection

# Methodology

## Methods Used to Collect/Select the Evidence

### Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

For varicella zoster virus, the PubMed database was searched using the following search headings: HIV, AIDS, herpes zoster, varicella.

For herpes simplex virus (HSV) infection, the PubMed database was searched under the following headings: HIV or AIDS and herpes simplex virus or HSV or genital herpes or HSV encephalitis or HSV CNS disease.

All information considered had to have been published in a peer review journal or presented at an international human immunodeficiency virus (HIV) meeting in abstract form. Inclusion/exclusion criteria essentially required that the information was relevant to the diagnosis, treatment or prevention of the specified opportunistic infection in HIV-positive individuals. Information of relevance to other related immunocompromised groups was also taken into consideration if the section authors felt relevant. Case reports were included and the review was not restricted only to clinical trials or meta-analyses. Search dates were from 1980 to January 2011.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Level of Evidence

Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Not stated

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Not stated

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Not stated

## Description of Method of Guideline Validation

Not applicable

## Evidence Supporting the Recommendations

### References Supporting the Recommendations

Balfour HH, Bean B, Laskin OL, Ambinder RF, Meyers JD, Wade JC, Zaia JA, Aeppli D, Kirk LE, Segreti AC, Keeney RE. Acyclovir halts progression of herpes zoster in immunocompromised patients. *New Eng J Med*. 1983 Jun 16;308(24):1448-53. [PubMed](#)

Brentjens MH, Torres G, He J, Lee PC, Tying SK. A double-blind randomized study of the use of 2 grams vs. 1 gram valacyclovir TID for 7 days in the treatment of acute herpes zoster in immunocompromised individuals. Abstract P455. In: 61st Annual Meeting of the American Academy of Dermatology; March 2003; San Francisco, CA, USA.

DeJesus E, Wald A, Warren T, Schacker TW, Trottier S, Shahmanesh M, Hill JL, Brennan CA. Valacyclovir for the suppression of recurrent genital herpes in human immunodeficiency virus-infected subjects. *J Infect Dis*. 2003 Oct 1;188(7):1009-16. [PubMed](#)

Dworkin RH, Johnson RW, Breuer J, Gnann JW, Levin MJ, Backonja M, Betts RF, Gershon AA, Haanpaa ML, McKendrick MW, Nurmikko TJ, Oaklander AL, Oxman MN, Pavan-Langston D, Petersen KL, Rowbotham MC, Schmader KE, Stacey BR, Tying SK, van Wijck AJ, Wallace MS, Wassilew SW, Whitley RJ. Recommendations for the management of herpes zoster. *Clin Infect Dis*. 2007 Jan 1;44(Suppl 1):S1-26. [243 references] [PubMed](#)

Hardy WD. Foscarnet treatment of acyclovir-resistant herpes simplex virus infection in patients with acquired immunodeficiency syndrome: preliminary results of a controlled, randomized, regimen-comparative trial. *Am J Med*. 1992 Feb 14;92(2A):30S-35S. [PubMed](#)

Romanowski B, Aoki FY, Martel AY, Lavender EA, Parsons JE, Saltzman RL. Efficacy and safety of famciclovir for treating mucocutaneous herpes simplex infection in HIV-infected individuals. Collaborative Famciclovir HIV Study Group. *AIDS*. 2000 Jun 16;14(9):1211-7. [PubMed](#)

Safrin S, Crumpacker C, Chatis P, Davis R, Hafner R, Rush J, Kessler HA, Landry B, Mills J. A controlled trial comparing foscarnet with vidarabine for acyclovir-resistant mucocutaneous herpes simplex in the acquired immunodeficiency syndrome. The AIDS Clinical Trials Group. *N Engl J Med*. 1991 Aug 22;325(8):551-5. [PubMed](#)

Saint-Leger E, Fillet AM, Malvy D, Rabanel B, Caumes E. [Efficacy of cidofovir in an HIV infected patient with an acyclovir and foscarnet resistant herpes simplex virus infection]. *Ann Dermatol Venereol*. 2001 Jun-Jul;128(6-7):747-9. [PubMed](#)

Shepp DH, Dandliker PS, Meyers JD. Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. *New Eng J Med*. 1986 Jan 23;314(4):208-12. [PubMed](#)

Snoeck R, Andrei G, Garsd M, Silverman A, Hedderman A, Balzarini J, Sadzot-Delvaux C, Tricot G, Clumeck N, De Clercq E. Successful treatment of progressive mucocutaneous infection due to acyclovir- and foscarnet-resistant herpes simplex virus with (S)-1-(3-

Sullivan M, Skiect D, Signs D, Young C. Famciclovir in the management of acute herpes zoster in HIV1 patients. Abstract 704. In: 4th Conference on Retroviruses and Opportunistic Infections; January 1997; Washington DC, USA.

## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate treatment of herpes viruses in human immunodeficiency virus (HIV)-seropositive individuals

### Potential Harms

Refer to Appendix 1 in the original guideline document for side effects of certain drug formulations.

## Contraindications

### Contraindications

Refer to Appendix 1 in the original guideline document for contraindications of certain drug formulations.

## Qualifying Statements

### Qualifying Statements

- These guidelines are primarily intended to guide practice in the United Kingdom and related health systems. Although it is hoped they can provide some guidance in developed countries there are some important distinctions in this environment and individual recommendations may not be as applicable in this setting.
- In the appendices in the original guideline document there is an A–Z of drugs used in the management of opportunistic infections. This is intended as a guideline but readers are advised to follow the discussion of dosing and the evidence for specific treatments provided in the text. In some cases alternative treatments are provided in the appendix in the original guideline document. These are not discussed in the text and these are mainly of historical interest and readers should be aware that these are not, in general, supported by the evidence base for treatments discussed in the text. It should also be noted that as evidence of drug toxicity, interactions, pregnancy risk and cost is rapidly evolving the table should be considered in association with the updated summary of product characteristics (SPC) for the agent and other relevant sources of drug information.
- Recommendations based upon expert opinion have the least evidence but perhaps provide an important reason for writing the guidelines: to produce a consensual opinion about current practice. It must, however, be appreciated that such opinion is not always correct and alternative practices may be equally valid. The recommendations contained in these guidelines should therefore be viewed as guidelines in the true spirit of the term. They are not designed to be restrictive nor should they challenge research into current practice. Similarly, although the British HIV Association (BHIVA) Opportunistic Infection Guidelines Group seeks to provide guidelines to optimize treatment, such care needs to be individualized and the authors have not constructed a document that they would wish to see used as a 'standard' for litigation.
- The clinical care of patients with known or suspected opportunistic infections (OIs) requires a multidisciplinary approach, drawing on the skills and experience of all healthcare professional groups. Moreover, these guidelines emphasize that inpatients with human

immunodeficiency virus (HIV)-related disease often need rapid access to a variety of diagnostic tests and radiological interventions that may not be immediately available at local hospitals. Furthermore, expert interpretation of these tests by supporting specialties such as radiology, histopathology, microbiology and virology is often required. Optimal care of opportunistic infection can only be achieved by the close cooperation of these healthcare professionals and unless all are intimately involved in the care of patients, it is likely that the outcome will be less favourable. In keeping with BHIVA standards for HIV clinical care, patients needing inpatient care for HIV-related disease should ordinarily be admitted to an HIV centre or the relevant tertiary service in liaison with the HIV centre.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Williams I, Leen C, Barton S. Herpes virus. In: British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011. HIV Med. 2011 Sep;12(Suppl 2):61-9. [84 references]

### Adaptation

Not applicable: The guideline is not adapted from another source.

## Date Released

2011 Sep

## Guideline Developer(s)

British HIV Association - Disease Specific Society

British Infection Association - Professional Association

## Source(s) of Funding

British HIV Association

## Guideline Committee

BHIVA Guidelines Writing Group on Opportunistic Infection

## Composition of Group That Authored the Guideline

*Section Authors:* I Williams, Royal Free and University College Medical School, London, UK; C Leen, Edinburgh University, UK; S Barton, Chelsea & Westminster Hospital, London, UK

*Group Joint Chair:* Dr Mark Nelson, Chelsea & Westminster Hospital, London, UK

*Group Joint Chair:* Professor David Dockrell, University of Sheffield, UK

*Group Joint Chair:* Dr Simon Edwards, Mortimer Market Centre, London, UK

*Writing Group Members:* Dr Brian Angus, John Radcliffe Hospital, Oxford, UK; Dr Simon Barton, Chelsea & Westminster Hospital, London, UK; Dr Nick Beeching, Liverpool School of Tropical Medicine, UK; Prof Colm Bergin, St James's Hospital, Dublin, Ireland; Dr Marta Boffito, Chelsea & Westminster Hospital, London, UK; Dr Ronan Breen, Royal Free Hospital, London, UK; Dr Jonathan Cartledge, Mortimer Market Centre, London, UK; Dr Susan Clarke, St James's Hospital, Dublin, Ireland; Dr Martin Fisher, Brighton and Sussex University Hospital, Brighton, UK; Dr Andrew Freedman, Cardiff University School of Medicine, UK; Prof Brian Gazzard, Chelsea & Westminster Hospital, London, UK; Dr Alison Grant, London School of Hygiene and Tropical Medicine, UK; Dr Julia Greig, Royal Hallamshire Hospital, Sheffield, UK; Dr Rachael Jones, Chelsea & Westminster Hospital, London, UK; Prof Saye Khoo, University of Liverpool; Prof Clifford Leen, Edinburgh University, UK; Dr Marc Lipman, Royal Free Hospital, London, UK; Dr Hadi Manji, National Hospital for Neurology & Neurosurgery, London, UK; Prof Robert Miller, Mortimer Market Centre, London, UK; Miss Suzanne Mitchell, Chelsea and Westminster Hospital, London, UK; Dr Ed Ong, Newcastle General Hospital, UK; Dr Anton Pozniak, Chelsea & Westminster Hospital, London, UK; Dr Matthias Schmid, Newcastle General Hospital, UK; Miss Marianne Shiew, Chelsea & Westminster Hospital, London, UK; Prof Mervyn Singer, University College London, UK; Dr Ed Wilkins, North Manchester General Hospital, UK; Dr Ian Williams, Royal Free and University College Medical School, London, UK; Dr Chris Wood, North Middlesex University Hospital, London, UK; Ms Rosy Weston, St Mary's Hospital, Imperial College, London, UK

## Financial Disclosures/Conflicts of Interest

The British HIV Association (BHIVA) has a clear policy of declarations of interests within the Association:

- BHIVA requires that all members of guidelines writing groups, as well as any expert external peer reviewers, must declare all interests and membership of other committees retrospectively on an annual basis, to give protection to individuals working as members of writing groups.
- All members of guidelines writing groups must undertake a declaration of interests prior to serving on a writing group and this declaration is confirmed and repeated at the publication of each set of completed guidelines published.
- The details given in declaration forms are retained on a register at the Secretariat and can be made available for publication, if required.

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the [British HIV Association \(BHIVA\) Web site](#) . Also available as a smartphone app from the [BHIVA Web site](#) .

## Availability of Companion Documents

None available

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on July 30, 2014.

## Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

## Disclaimer

### NGC Disclaimer

The National Guideline Clearinghouse<sup>®</sup> (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion-criteria.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.